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OSWALD T. AVERY AND THE COPLEY MEDAL
OF THE ROYAL SOCIETY

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In all celebrations surrounding the 50th anniversary of the famous 1944 paper of Avery, MacLeod, and McCarty on the chemical nature of the transforming substance [1], reference is frequently made to the Copley Medal of the Royal Society, awarded to Avery in 1945. It may be of some historic interest, therefore, to enquire into the nature of the Copley Medal and the reasons given by the Society in awarding it to Avery, since the Society is sometimes credited for having rapidly recognized the signal importance of Avery's work.

The Copley Medal has long been regarded as "the highest scientific distinction that the Royal Society has to bestow" [2]. It was made possible by the legacy of 100 pounds from Sir Godfrey Copley, Bart., F.R.S., in 1709. The prize was originally intended to be laid out in experiments for the benefit of the Society. In 1736, Martin Folkes, subsequently President of the Society, suggested that "a medal or other honorary prize should be bestowed on the person whose experiment should be best approved, by which means he apprehended a laudable emulation might be excited among men of genius to try their invention, whom, in all probability, may never be moved for the sake of lucre" [2].

The terms of the prize were modified in 1831, when it was resolved that a medal be awarded "to the living author of such philosophical research, either published or communicated to the Society as may appear to the Council to be deserving of that honour." The weight of the medal was fixed at "1 oz, 2 dwts of fine gold." The awardees have included Benjamin Franklin in 1753, Joseph Priestly in 1772, Sir Humphry Davy in 1805,

The author acknowledges the assistance of Mary Sampson Archivist/The Royal Society and the advice and encouragement of Maclyn McCarty.

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Note: The correspondence regarding Avery and the Royal Society are to be found in the Dale Papers [93HD.6.12-24]

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0031-5982/96/3901-0945 \$01.00

Charles Darwin in 1925, and Niels Bohr in 1926, and James Watson and Crick in 1969, and from many other scientists.

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Charles Darwin in 1864, Ivan Petrovich Pavlov in 1915, Albert Einstein in 1925, and Niels Bohr in 1938. More recently, the prize was awarded to Peter Medawar in 1969, Frederick Sanger in 1977, Cesar Milstein in 1989, and James D. Watson in 1993. Indeed, luminaries from all branches of science and from many countries have been accorded this honor [3, 4].

At a meeting of the Council of the Society on 17 June 1943, preliminary consideration was given to the award of the Copley Medal for 1943. Avery was among five of the names suggested for the receipt of the Medal. Other suggestions included the well-known physiologist Sir Joseph Barcroft and the American physicist, later Nobel Prize Winner, Percy W. Bridgman [5]. In the event, Avery was not recommended for the Copley Medal. On 15 June 1944, however, four months after the publication of Avery's epoch-making paper (co-authored by MacLeod and McCarty) entitled "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types" in the *Journal of Experimental Medicine* [1], Avery was among the five scientists proposed by Sir Henry Dale and seconded by Sir Thomas Lewis for the Copley Medal. The citation was brief and followed closely the write-up of Paul G. Fildes: "His pioneer work on immunity, with special reference to the relationship of chemical composition and structure on the immunological specificity of naturally-occurring antigens of bacterial origin" [6]. But again, Avery failed to be awarded the Medal.

Just two months earlier, on 20 April, Avery was "recommended as a proper person to be placed on the list of Foreign Members of the Royal Society." His 21 backers included Henry Dale, A. V. Hill, and Thomas Lewis, as well as the microbiologists Percival Hartley and Paul Fildes. Interestingly, Avery's nomination contained no mention of the transformation paper. The official citation for his election, almost certainly prepared by Fildes, was quite general and was for "his pioneer work on the bacteriology and on the chemical nature of antigenic structure" [7]. In an extended memorandum in support of Avery's nomination for membership, Fildes began by asserting that Avery was "the senior American bacteriologist of the day." His work began, Fildes went on to write, in 1913, when working with his colleague Alphonse Dochez on "the antigenic structure of pneumococcus by familiar serological methods." When, in 1923, he interested Heidelberger and a number of other chemists, "a new field in serology" opened up [6]. Avery's work, Fildes continued, "originated in a recognized attack on respiratory diseases in which he was the leader" [6]. Again, no mention of transformation. However, unlike the delay in awarding Avery the Copley Medal, his election to the Society was favorably acted upon on 15 June 1944.

The day before Avery was elected to the Society, he was nominated for the Copley Medal for the third time. Finally, on 8 November 1945, the Copley Medal was awarded to "Dr. O. T. Avery in recognition of his success

in introducing chemical methods in the study of immunity against infective diseases." The continued omission of any reference to transformation (it was now 21 months since the paper on transformation was published) was finally rectified in a long memorandum from Sir Percival Hartley, in which he elaborated on Fildes's original write-up:

In February 1944, after many years of patient labor and persistent endeavour, Avery with his colleagues, MacLeod and McCarty, announced the discovery of the substance, almost certainly a nucleic acid of the deoxyribose type, which, in minute quantities, is capable of inducing an *in vitro* transformation of a rough, unencapsulated, avirulent pneumococcus of one type (II) into a smooth, encapsulated, virulent pneumococcus of another type (III)—a biological change which is chemically induced and specifically directed by a known chemical substance. The interest and importance of this work, to chemists and biologists (and perhaps most of all to geneticists) is outstanding: it represents fundamental research of the highest merit, and to those familiar with Avery's life work this paper, published on the eve of his retirement, will be judged by many to be his greatest achievement. [8]

The importance of transformation was now fully recognized.

Hartley had reason to know the work of Avery's laboratory but in a different connection. Hartley had noted that guinea pigs could not be made anaphylactic to a pneumococcal polysaccharide from the injection of a specific precipitin obtained from an immunized horse. But before Hartley had time to publish these results, Avery and Tillett had shown that guinea pigs could be sensitized against polysaccharide by prior injection, if the corresponding precipitin was obtained from an immunized rabbit and also showed, as had Hartley, that this did not occur if it was a horse that had been immunized [9].

On 30 November 1945, on the occasion of the anniversary meeting of the Royal Society, Sir Henry Dale, President of the Society, had now read Hartley's brief, and the profound significance of the 1944 paper had become publicly proclaimed. In a scholarly account of Avery's life's work, and with full acknowledgment of the earlier contribution of Fred Griffith, who had discovered the phenomenon of transformation by showing that heat-killed virulent pneumococci could convert a nonvirulent strain to one that was virulent, Dale went on to say:

Here surely is a change to which, if we were dealing with higher organisms, we should accord the status of a genetic variation; and the substance inducing it—the gene in solution, one is tempted to call it—appears to be a nucleic acid of the deoxyribose type. Whatever it be, it is something which should be capable of complete description in terms of structural chemistry.

It has been a matter for rejoicing to his many admirers, friends, and followers in many countries that Avery, a veteran now among investigators, should thus, on the eve of his retirement, have attained this new peak of discovery—a fitting climax to a devoted career of such wide influence on the progress of science. [10]

In McCarty's classical account of the discovery that DNA was the transforming principle, Avery's modesty, even shyness, is consistently apparent.

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He disliked any personal limelight and preferred remaining quietly in his laboratory working with his close colleagues, to lecturing and attending scientific meetings. Avery was notified of the impending award on 8 November 1945, and was invited to attend the anniversary meeting of the Society, which was to be held on 30 November, to receive the medal. He declined. In a short but gracious telegram he expressed regret that "compelling circumstances" made it impossible for him to attend the anniversary meeting. The Society was evidently disappointed, but wrote saying that the award would be accepted on his behalf by the American Ambassador or his delegate, who in turn would be responsible for delivering the medal to Avery. There was one additional administrative matter to be settled.

The award carried with it not only the Copley Medal, no longer gold, but silvergilt, but an honorarium of 35 pounds, and the assistant Secretary of the Society wrote to Avery, on 6 December 1945, requesting the name of Avery's bank so that the money could be deposited in his account. Avery characteristically did not respond, even though a second letter was sent on 16 February 1946, again requesting a reply. It was not until 31 November 1946, however, that Avery finally replied, asking that the money be "transferred to some British fund devoted to the advancement of research in the field of medicine and related science," and he asked that he would prefer the gift to be anonymous "as from a Foreign Member of the Royal Society." The Society, after pondering the allocation of the money, decided that it should be transferred to the Society's "Special Research Fund," which dealt with research in the tropics and tropical disease and which was "not very well off." A. V. Hill, the Foreign Secretary of the Society, wrote to Avery on 20 December 1946, informing him of the decision and thanking him for "the friendly thought behind the gift," closing the letter by wishing Avery all best wishes for Christmas and the New Year.

As with so many aspects of Avery's personal life, additional details are sketchy. It seems probable that Avery received the medal from the American Ambassador in New York, but no details of that event are available. Later, Dale visited Avery at the Rockefeller Institute in New York, but the exact date and the nature of their conversation remain unknown. Certainly, Avery greatly appreciated the award, perhaps more than most that came his way. His failure to attend the anniversary meeting was intended as no disrespect nor lack of pleasure in the award. Avery, as mentioned earlier, was not overly keen on travel and, as McCarty points out in his book, Avery did not even journey to Cambridge when invited to receive an honorary degree from the University [11].

Avery received many awards during his life, and he prized the Copley Medal and foreign membership in the Royal Society greatly, for he was something of an anglophile. However, as Dubos wrote in his obituary of Avery in the *Biographical Memoirs of the Royal Society* in 1956, it "remains to this day, a matter of painful surprise that Avery was not awarded a Nobel

Prize" [12]. The surprise Dubos expressed still remains. The discovery that DNA was the genetic material remains the most fundamental biological discovery of the 20th century.

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